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noted that Quay teaches microbubbles comprising selected gases or mixtures thereof. Finally, the PTO cited Schneider et al. as teaching microbubbles comprising two gases encapsulated in a proteinaceous shell. The PTO reasoned that it would have been obvious to one of ordinary skill in the art to combine these references to achieve the microbubbles used in the methods of the claimed invention. The PTO then concluded that if the microbubbles themselves are obvious, then claims to methods of using those microbubbles are obvious. Applicants respectfully traverse this rejection as applied to the amended claims.

The cited art, alone or in combination, fails to teach or suggest all the claimed limitations. Amended Claims 62, 109, and 123, now recite a gas osmotic agent and a non-fluorocarbon modifier gas present in a microbubble in a fixed molar ratio that stabilizes the microbubble. Microbubbles of the present invention can be prepared so as to produce an internal osmotic pressure that is capable of counteracting the Laplace pressure produced by the surfactant surrounding the bubble, thus stabilizing the bubble. Not all ratios of gases will provide this result; thus, the claims are limited to only those fixed ratios that counteract the Laplace pressure with osmotic pressure. These claimed features are completely absent from the cited art and therefore distinguish the pending claims from the cited art.

A review of the cited art shows that these references fail to teach the limitations of the pending claims. For example, the PTO cites Lambert as teaching soluble and relatively insoluble gases that could be combined by one or ordinary skill in the art to achieve the claimed invention. However, Lambert does not teach or suggest the gas mixtures in molar ratios that are capable of stabilizing microbubbles. At best, Lambert merely mentions gases that might be mixed. Beyond the mere mention of gas mixtures, the cited art is silent as to the ratio of the gases found in these mixtures and is further silent as to an appropriate ratio of gases required to produce the stabilized microbubbles of the above-referenced application.

Further, none of the other references cited by the PTO teach a combination of gases in a fixed molar ratio that results in a stabilized microbubble. Quay only discusses gas solubility and does not teach the importance of gas ratios that result in microbubble stabilization. The Schneider et al. reference is similarly silent concerning the importance of gas ratios for microbubble stabilization.

At most, the PTO could argue that the prior art unwittingly discloses a generic concept; i.e., a mixture of gases, without disclosing any particular species and without disclosing or even

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appreciating the possibility of osmotic stabilization. It is well established that such an unwitting disclosure does not inherently disclose a feature of a subsequently-claimed invention unless the prior art necessarily and always provides that feature. A prior art disclosure of mixtures in general does not necessarily and always lead one to use a fixed ratio of gases that will provide sufficient osmotic pressure to counteract the Laplace pressure. Thus, the claimed feature is not disclosed in the cited prior art.

Similarly, one could analyze the question from the perspective of genus-species law. It is well established that the prior art disclosure of a genus (e.g., mixtures in general) does not make obvious a later claim to a species (e.g., a particular ratio) within that genus that has unexpected properties.

Under either an inherency analysis or a genus-species analysis, the art cited by the PTO fails to teach all the limitations of the claimed invention. Therefore, a *prima facie* case of obviousness has not been made. Accordingly, Applicants respectfully request withdrawal of the pending rejection.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. Nevertheless, the PTO is invited to contact the undersigned at the telephone number appearing below to discuss any remaining issues the may exist.

Respectfully submitted,

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